

CLAIM AMENDMENT

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended): Edible plant material comprising transgenic legume plant cells transformed with a resveratrol synthase transgene under the control of a constitutive promoter whereby said transgenic legume plant cells accumulate resveratrol glucoside upon expression of said resveratrol synthase transgene, wherein said edible plant material exhibits an increased concentration of resveratrol glucoside as compared to edible plant material consisting of non-transgenic plant cells of the same cell type grown under the same conditions.
2. (Previously presented): The edible plant material of Claim 1, wherein said edible plant material is suitable for consumption as a food stuff, a nutritional supplement, an animal feed supplement, or a nutraceutical in the form of a live or harvested whole plant or plant part.
3. (Previously presented): The edible plant material of Claim 1, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.
4. (Previously presented): The edible plant material of Claim 2, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.
5. (Canceled)
6. (Currently amended): The edible plant material of Claim 15, wherein said plant is alfalfa.
7. (Currently amended): The edible plant material of Claim 15, wherein said plant is soybean.

8. (Currently amended): A composition comprising edible plant material, said edible plant material comprising transgenic legume plant cells transformed with a resveratrol synthase transgene under the control of a constitutive promoter whereby said transgenic legume plant cells accumulate resveratrol glucoside upon expression of said resveratrol synthase transgene, wherein the percentage of resveratrol glucoside in said composition obtained by adding a given weight of said edible plant material comprising said transgenic legume plant cells to said composition is higher than the percentage of resveratrol glucoside obtainable by adding instead the same weight of edible plant material consisting of non-transgenic plant cells of the same cell type grown under the same conditions to said composition.
9. (Previously presented): The composition of Claim 8, wherein said composition is suitable for consumption as a food stuff, a nutritional supplement, an animal feed supplement, or a nutraceutical.
10. (Previously presented): The composition of Claim 8, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.
11. (Previously presented): The composition of Claim 9, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.
12. (Canceled)
13. (Currently amended): The composition of Claim 812, wherein said plant is alfalfa.
14. (Currently amended): The composition of Claim 812, wherein said plant is soybean.
15. (Currently amended): An edible legume plant comprising transgenic legume plant cells transformed with a resveratrol synthase transgene under the control of a constitutive promoter whereby said transgenic legume plant cells accumulate resveratrol glucoside

upon expression of said resveratrol synthase transgene, wherein said edible legume plant exhibits an increased concentration of resveratrol glucoside as compared to an edible legume plant comprising non-transgenic plant cells of the same cell type grown under the same conditions.

16. (Currently amended): The edible legume plant of Claim 15, wherein said edible plant is suitable for consumption as a food stuff, a nutritional supplement, an animal feed supplement, or a nutraceutical in the form of a live or harvested whole plant or a plant part.
17. (Currently amended): The edible legume plant of Claim 15, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.
18. (Currently amended): The edible legume plant of Claim 16, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.
- 19-21. (Canceled)
22. (Currently amended): The edible legume plant of Claim 1524, wherein said plant is alfalfa.
23. (Currently amended): The edible legume plant of Claim 1524, wherein said plant is soybean.
24. (Currently amended): Seed from the edible legume plant of Claim 15, 16, 17 or 18 which comprises said resveratrol synthase transgene.
25. (Currently amended): Progeny from the edible legume plant of Claim 15, 16, 17 or 18 which comprises said resveratrol synthase transgene.

26. (Currently amended): Progeny from the seed of Claim 24 which comprises said resveratrol synthase transgene.

27-28. (Canceled)

29. (Currently amended): A method of using an edible legume plant comprising

transforming plant cells of said edible legume plant with a resveratrol synthase transgene under the control of a constitutive promoter to form transgenic plant cells whereby said transgenic plant cells accumulate resveratrol glucoside upon expression of said resveratrol synthase transgene, wherein said edible legume plant exhibits an increased concentration of resveratrol glucoside as compared to an edible legume plant comprising non-transgenic plant cells of the same cell type grown under the same conditions and consuming said edible legume plant to provide a nutraceutical benefit to a human or animal.

30. (Previously presented): The method of Claim 29, wherein said open reading frame encodes the amino acid sequence of SEQ ID NO:2.

31-38. (Canceled)

39. (Currently amended): A method of increasing disease resistance in an edible legume plant comprising transforming cells of said plant with a resveratrol synthase transgene under the control of a constitutive promoter whereby said transgenic plant cells accumulate resveratrol glucoside upon expression of said resveratrol synthase transgene, wherein said edible legume plant exhibits an increased concentration of resveratrol glucoside as compared to an edible legume plant comprising non-transgenic plant cells of the same cell type grown under the same conditions.

40. (Previously presented): The method of Claim 39, wherein said open reading frame encodes the amino acid sequence of SEQ ID NO:2.
- 41-57. (Canceled)
58. (Currently amended): Seed from the edible legume plant of Claim 21 which comprises said resveratrol synthase transgene.
59. (Currently amended): Seed from the edible legume plant of Claim 22 which comprises said resveratrol synthase transgene.
60. (Currently amended): Seed from the edible legume plant of Claim 23 which comprises said resveratrol synthase transgene.
61. (Currently amended): Progeny from the edible legume plant of Claim 21 which comprises said resveratrol synthase transgene.
62. (Currently amended): Progeny from the edible legume plant of Claim 22 which comprises said resveratrol synthase transgene.
63. (Currently amended): Progeny from the edible legume plant of Claim 23, which comprises said resveratrol synthase transgene.
64. (Currently amended): Progeny from the seed of Claim 21 which comprises said resveratrol synthase transgene.
65. (Currently amended): Progeny from the seed of Claim 22, which comprises said resveratrol synthase transgene.

66. (Currently amended): Progeny from the seed of Claim 23 which comprises said resveratrol synthase transgene.
67. (Currently amended): The edible plant of Claim 15, wherein said edible legume plant is useful as a source for isolated resveratrol glucoside.

RESPONSE TO OFFICE ACTION**A. Status of the Claims**

Claims 1-67 were filed. Claims 5, 12, 19-21, 27-28, 31-38 and 41-57 have been canceled without prejudice or disclaimer. Claims 1-4, 6-11, 13-18, 22-26, 29-30, 39-40, and 58-67 and therefore now pending and presented herein for reconsideration.

B. Rejection of Claims Under 35 U.S.C. §112, First Paragraph

The Action rejects claims 1-5, 8-12, 15-18, 21, 24-30, 34-36, 39-42, 58, 61, 64 and 67 under 35 U.S.C. §112, first paragraph, as not being enabled. The rejection is made on the basis that not all plants accumulate resveratrol glucoside upon the expression of a resveratrol synthase transgene. It is asserted in particular that plants such as tobacco do not possess an endogenous glucosyl transferase capable of transforming resveratrol to produce resveratrol glucoside, and thus, although it has been shown that plants such as alfalfa and soybean do have that activity, it has not been shown which other plants would be capable of doing so.

In response, Applicants respectfully traverse but note that the current claims specify transgenic legume plants that accumulate resveratrol glucoside upon expression of resveratrol synthase transgene. As indicated in the Action, Applicants have already shown that legume plants such as alfalfa and soybeans contain the requisite enzymes such as glucosyl transferases, as well as metabolic precursors to accumulate resveratrol glucoside upon expression of resveratrol synthase transgene. The rejection is therefore now moot in light of the amendment and removal thereof is respectfully requested.

B. Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

The Action rejects claims 27, 34 and 41 under 35 U.S.C. §112, second paragraph, as being indefinite. In particular it is stated that the step of cultivating and minimizing the concentration of β -glucosidase active on resveratrol glucoside is indefinite because the metes and bounds of this limitation are unclear. In response, Applicants respectfully traverse but note that the claims have been canceled as this step is already inherent in the instantly claimed legume plants. The rejection is thus now moot and removal thereof is respectfully requested.

C. Rejection of Claims Under 35 U.S.C. §102(a)

The Action rejects the claims as anticipated over Fischer (December 1994, Doctoral Dissertation) taken with evidence of Kobayashi *et al.* (2000, *Plant Cell Reports* Vol. 19, p904-910). It is stated in particular that Fischer teaches tobacco plants transformed with a nucleic acid encoding peanut resveratrol synthase linked to a constitutive promoter and that Kobayashi *et al.* demonstrates that the tobacco plant would inherently produce resveratrol glucosides.

In response Applicants note that the current claims are directed to transgenic legumes. The Action has not alleged that this subject matter is taught or suggested by Fisher and thus all elements of the claims are not present in the prior art as is required to maintain a §102 rejection.

In view of the foregoing, removal of the rejection is respectfully requested.

D. Rejection of Claims Under 35 U.S.C. § 103

(1) The Action rejects the claims as being obvious under 35 U.S.C. § 103 over Schroder *et al.* (U.S. Patent No. 5,689,046) in view of Fischer (December 1994, Doctoral Dissertation) and further in view of Tropf *et al.* (1994, *J. Mol. Evol.*, 38:610-618). It is stated in particular that the

asserted success of Fischer in constitutively expressing a peanut resveratrol synthase in tobacco would provide the motivation and reasonable expectation of success for the expression of such a gene in soybeans and alfalfa. Further, the Action argues that Tropf teaches a transgene encoding the amino acid sequence of SEQ ID NO:2, and that Applicants admitted that the transgene taught by Tropf encodes the amino acid sequence of SEQ ID NO: 2. Applicants respectfully traverse.

In response it is first noted that none of the references have been shown to teach expression in legumes, as recited by the claims. All of the elements have therefore not been shown in the prior art as must specifically be done to support a rejection under 35 U.S.C. §103.

Further, the Fischer reference, which is the reference alleged to teach the desirability of heterologous expression of resveratrol synthase based on alleged success in tobacco, actually provides teaching away from constitutive promoters as recited in the claims. For example, on page 1 of the English translation of Fischer it is stated that as far as constitutive expression of the peanut STS gene was concerned in tobacco protoplasts "a cytotoxic effect of consistently high stilbene concentrations may definitely be plausible." This is supported on page 4 of the translation, which cites observations indicating that "high STS activities or resveratrol concentrations have a cell-damaging effect." Further, on page 5, it is indicated that constitutive expression of the chimeric STS gene from peanut in tobacco has not led to identification of very strong expressing clones whereas inducible expression was very successful. In fact on page 9, it is indicated that an increase in resistance to fungi was only observed by inducible expression, and in fact constitutive expression can lead to male sterility. The reference therefore provides teaching away from the claimed invention.

Still further, the instant claims are directed to legume plants and not tobacco plants. Tobacco and legume plants are substantially genetically diverged. A simple conclusion that

studies involving tobacco provide the motivation and expectation of success in arriving at the claimed invention is not tenable. This was plainly illustrated by the Federal Circuit in a case dealing directly with tobacco in *Adang v. Fischhoff*, 286 F.3d 1346, 62 U.S.P.Q.2D 1504 (Fed. Cir. 2002). In *Adang*, the Federal Circuit considered whether a patent application disclosing transgenic tobacco plants encoding Bt and exhibiting toxicity to Lepidopterans would enable insecticidal tomatoes expressing a full length Bt when combined with contemporaneous publications and a citation in the application to a method for transforming tomatoes. *Id.* at 1350. Citing evidence submitted showing that bioassays could vary even among different strains of tobacco, the Federal Circuit cited the conclusion of the earlier Board decision that:

persons skilled in the art **would not have expected success** in regenerating **tomato** plants insecticidal to Lepidopteran insects from dicotyledonous tomato plant cells transformed by a full length Bt crystal protein gene based on evidence that **tobacco** cells had been successfully transformed by the same genetic construct and one strain of dicotyledonous tobacco plants insecticidal to Lepidopteran insects had been regenerated therefrom.

(emphasis added) (*Id.* at 1350)

The court therefore found it "reasonable to conclude that those of skill in the art would **not have expected** expression in **tomato** plants to track that in a particular strain of **tobacco**." (emphasis added) *Id.* The court further held that citation to a general method for transformation of tomato did not remedy the deficiencies of the *Adang* patent application, given the unpredictable nature of the claimed subject matter. *Id.* at 1358. As in the current case, it is a complete oversimplification unsupported in science or law to state that studies in tobacco with a given gene provide the motivation and expectation in success in expressing the gene in diverged species such as legumes, regardless of any constructs or general transformation methods for legumes that may have existed.

Finally, Applicants note that non-obviousness is affirmatively demonstrated by the studies in the specification. Specifically, Example 3 of the specification describes studies showing that accumulation of resveratrol glucoside in transgenic alfalfa expressing stilbene synthase with a constitutive promoter was sufficient to result in *inhibition of colon carcinogenesis* in mice fed the dried transgenic alfalfa. Such a health benefit demonstrated in an *in vivo* model is indeed a surprising and unexpected result fully demonstrating the non-obviousness of the claims. MPEP § 716.02(a). Nothing in the prior art suggests that such a significant health benefit could be obtained. Non-obviousness is thus demonstrated on this basis alone, not to mention the foregoing comments.

In conclusion, the claims are not properly rejected as obvious at least because: (1) there was no motivation or suggestion to combine the references; (2) there was no reasonable expectation of success in the art to arrive at the invention; and (3) Applicants have demonstrated unexpected results. Applicants therefore respectfully request removal of the rejection under 35 U.S.C. § 103.

(2) Claims 1-18, 21-42, and 58-67 stand rejected under § 103(a) as unpatentable over Schroder in view of Comai, and further in view of Tropf, Leekband and Lorz, and Applicants' asserted admission. In particular, the Action alleges that it would have been obvious to modify the resveratrol synthase transgene of Schroder with the promoter of Comai to constitutively express a resveratrol transgene in a transgenic plant. Further, the Action argues that Tropf teaches a transgene encoding the amino acid sequence of SEQ ID NO:2, and that Applicants admitted that the transgene taught by Tropf encodes the amino acid sequence of SEQ ID NO: 2. The Action also states that Leekband and Lorz teach that it was obvious to operably link a

constitutive promoter to a resveratrol synthase gene and transform a plant. Applicants traverse this rejection.

In response it is first noted that none of the references have been shown to teach expression in legumes, as recited by the claims. All of the elements have therefore not been shown in the prior art as must specifically be done to support a rejection under 35 U.S.C. §103.

Applicants further note that the comments maintaining the instant rejection rely on an "obvious to try" type rationale explicitly rejected by the Federal Circuit. Specifically, it is asserted that the claims are obvious, despite the lack of any teaching of a reasonable success in arriving at the claimed invention, because it allegedly would have been "obvious to do" instead of obvious to try. Action at p. 11. These comments however ignore the fact that there is no basis in the prior art to suggest a reasonable expectation that the recited sequences could be *expressed* in legumes for any advantage as recited in the claims. Despite comments in the Action asserting that any conclusion on obviousness is in a sense necessarily a reconstruction based on hindsight, this hindsight is in fact all that is used to support the rejection. No evidence whatsoever providing a reasonable expectation and motivation for the expression of a resveratrol synthase gene for benefit has been provided.

Given the complexity of successfully introducing and expressing a particular coding sequence, particularly with heterologous combinations of expression elements not found in nature, an expectation of success in expressing a resveratrol synthase gene from a heterologous constitutive promoter would have been absent but for the teaching of Applicants' disclosure. As set forth above, expression in tobacco does not provide a motivation and expectation of success in doing so in legumes, and the prior art specifically teaches the problems found by others in constitutively expressing resveratrol synthase. A basis has simply not been presented in the cited

art for concluding that one of skill in the art would have a reasonable expectation that transgenic plant cells would accumulate resveratrol glucoside upon expression of the constitutively expressed resveratrol synthase transgene. Both the motivation to combine and reasonable expectation of success must be found in the cited prior art or in the knowledge generally available to one of skill in the art, not in Applicants' specification. See *In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991), see also, M.P.E.P. § 2142. Such evidence is lacking here and therefore the rejection under §103 must be removed. *In re Carroll*, 202 USPQ 571 (CCPA 1979).

Finally, with respect to the assertion that unexpected results have not been demonstrated because a declaration under 37 C.F.R. §1.132 was not submitted, Applicants note that such evidence is found in the *specification* and thus need not be submitted by Declaration. Specifically, the inventors showed in *Example 3* of the specification that accumulation of resveratrol glucoside in transgenic alfalfa expressing stilbene synthase with a constitutive promoter was sufficient to result in *inhibition of colon carcinogenesis* in mice fed the dried transgenic alfalfa. Such a health benefit as this demonstrated in an *in vivo* model is indeed a surprising and unexpected result fully demonstrating the non-obviousness of the claims. MPEP § 716.02(a).

In conclusion, the claims are not properly rejected under 35 U.S.C. § 103 at least because: (1) there was no motivation or suggestion to combine the references; (2) there was no reasonable expectation of success; and (3) the present invention provided unexpected results. Applicants therefore respectfully request removal of the rejection.

E. Conclusion

This is submitted to be a complete response to the referenced Office Action. In conclusion, Applicant submits that, in light of the foregoing remarks, the present case is in condition for allowance and such favorable action is respectfully requested.

The Examiner is invited to contact the undersigned at (512)536-3085 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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